HUMAN MONOCLONAL ANTIBODIES CROSS-REACTING TO INSULIN-LIKE GROWTH FACTORS IGF-I AND IGF-II AS POTENTIAL ANTI-TUMOR AGENTS

SUMMARY

The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to co-develop, evaluate, or commercialize monoclonal antibodies to IGF-1 and IGF-II for the treatment of cancer.

REFERENCE NUMBER

E-068-2011

PRODUCT TYPE

- Therapeutics

KEYWORDS

- metastasis
- monoclonal antibody
- insulin-like growth factor
- IGF-I
- IGF-II

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to co-develop, evaluate, or commercialize this technology.

The type 1 insulin-like growth factor (IGF) receptor (IGF1R) is over-expressed by many tumors and mediates proliferation, motility, and protection from apoptosis. Agents that inhibit IGF1R expression or function can potentially block tumor growth and metastasis. Its major ligands, IGF-I, and IGF-II are over-expressed by multiple tumor types. Previous studies indicate that inhibition of IGF-I, and/or IGF-II

binding to its cognizant receptor negatively modulates signal transduction through the IGF pathway and concomitant cell proliferation and growth. Therefore, use of humanized or fully human antibodies against IGFs represents a valid approach to inhibit tumor growth.

The present invention discloses the identification and characterization of a fully human monoclonal antibody designated m708.5 that has been affinity maturated against IGF-I and IGF-II and displays extremely high affinities for IGF-I and IGF-II in the picoM range. The m708.5 antibody potently inhibited signal transduction mediated by the IGF-1R interaction with IGF-I and IGF-II and blocked phosphorylation of IGF-IR and the insulin receptor. Further, this antibody inhibited migration in the MCF-7 breast cancer cell line at the picoM range. Therefore, this antibody can be used to prevent binding of IGF-I and/or IGF-II to its concomitant receptor IGFIR, consequently, modulating diseases such as cancer.

POTENTIAL COMMERCIAL APPLICATIONS

- Therapeutic for the treatment of various human diseases associated with aberrant cell growth and motility such as breast, prostate, and leukemia carcinomas.
- Research regent to study IGF-I and/or IGF-II binding and its association with tumor growth.

COMPETITIVE ADVANTAGES

- Antibodies against the ligands IGF-I and IGF-II, such as this invention, inhibit the interaction with IGF-IR yet likely do not have the type of toxicity associated with IGF-1R antibodies.
- High concentrations of IGF-II are found in cancer patients, on average several fold higher than IGF-I, thus this cross-reacting IGF-I/IGF-II antibody could be more effective than existing IGF-IR and/or IGF-I currently in the clinic.
- This novel IGF antibody may provide therapeutic intervention for multiple carcinomas.

INVENTOR(S)

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DEVELOPMENT STAGE

- Discovery (Lead Identification)

PUBLICATIONS

1. Zhao Q, et al. Human monoclonal antibody fragments binding to insulin-like growth factors 1 and 2 with picomolar affinity. Mol Cancer Ther. 2011 Jul 12; Epub ahead of print. [PMID 21750218]
2. Feng Y, et al. Novel human monoclonal antibodies to insulin-like growth factor (IGF)-II that potently inhibit the IGF receptor type I signal transduction function. Mol Cancer Ther. 2006;5(1):114-120. [PMID 18283605]
3. Kimura T, et al. Targeting of bone-derived insulin-like growth factor-II by a human neutralizing antibody suppresses the growth of prostate cancer cells in a human bone environment. Clin Cancer Res.

2010 Jan 1;16(1): 121-129. [PMID 20028742]

PATENT STATUS

- **U.S. Filed:** U.S. Provisional Application No. 61/474,664 filed 12 April 2011
- **Foreign Filed:** PCT Application No. PCT/US2012/033128 filed 11 April 2012

RELATED TECHNOLOGIES

- E-217-2005
- E-336-2005

THERAPEUTIC AREA

- Cancer/Neoplasm